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ACCURACY OF ENDOMETRIAL BIOPSY DATING IN RELATION TO THE MIDCYCLE LUTEINIZING HORMONE PEAK

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The accuracy of endometrial biopsy dating was evaluated in a selected group of apparently normal women in whom the basal body temperature (BBT), the onset of subsequent menstruation, the midcycle luteinizing hormone (LH) peak, and the 17β-estradiol peak were determined. Forty-two women with regular cycles, normal ovaries at laparoscopy, and luteal phases of 12 to 15 days were studied. In group I (n = 20), the infertility could be explained satisfactorily by either tubal occlusion or infertility of the husband, while in group II (n = 22) no explanation was found for the infertility. In group I, the duration of the luteal phase, defined as the interval between the LH peak and the onset of subsequent menstruation, was 13.4 ± 0.7 days. The plasma 17β-estradiol concentration declined ($P < 0.01$) on the day of the LH peak in both groups of women, while the first significant rise ($P < 0.05$) in BBT occurred in groups I and II, respectively, 1 and 2 days following the LH peak. Dating of the endometrial biopsy correlated with the LH peak with standard deviations of 1.2 and 1.3 days, respectively, in groups I II.

It is suggested that, in women with a progressive rise in BBT over several days, the localization of the LH peak can be helpful for correct interpretation of the endometrial biopsy.

Since the introduction of histologic dating of endometrial biopsies by Rock and Bartlett in 1937,[1] the method has been widely used for evaluation of luteal function in infertile patients.[2-4] The method as evaluated by Noyes and Haman,[5] in which basal body temperature (BBT) charts and onset of menstruation are used as points of reference, was found to be accurate to ± 1 day. Because the determination of the exact time of ovulation by BBT recording is known to be imprecise, this study was undertaken to test the accuracy of histologic dating of the luteal phase as related to accurate timing of ovulation by the midcycle LH peak and maximal plasma levels of 17β-estradiol.

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MATERIALS AND METHODS

Eighty-two couples with primary or secondary infertility were investigated according to a comprehensive scheme. The investigation included clinical examination of both partners, sperm analyses, assay of spermagglutinins, postcoital tests, recordings of BBT for periods of at least 3 months, endometrial biopsies, hysterosalpingography, laparoscopy, progesterone assays during the luteal phase, preovulatory 17β-estradiol assays, and localization of the LH peak. In each cycle selected for endometrial biopsy, daily blood samples were obtained from day 9 to day 17 for

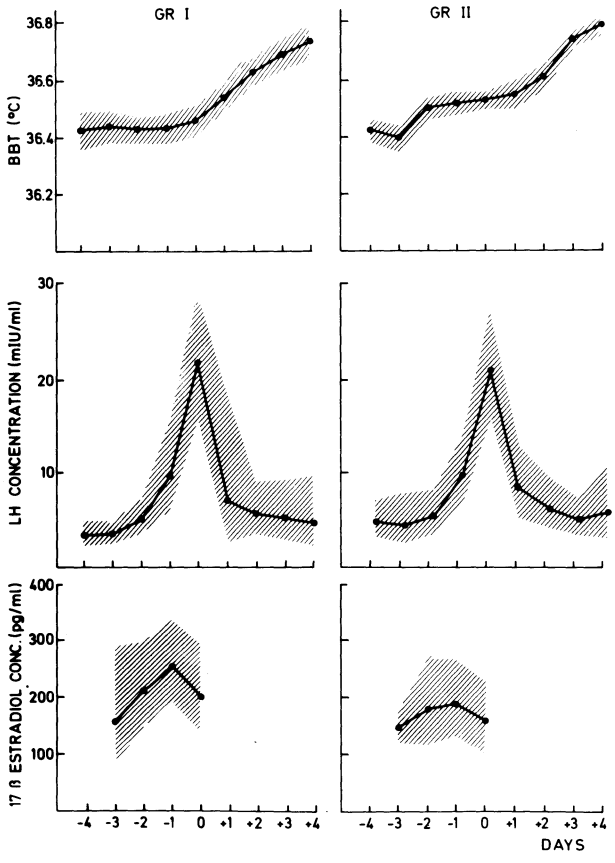

FIG. 1. Basal body temperature (mean ± 1 SE), plasma LH (mean ± 1 SD), and plasma 17β-estradiol (mean ± 1 SD) concentrations in group I (control group) and group II (women with unexplained infertility).

determination of 17β-estradiol and LH levels; in the latter half of the cycle the biopsy was performed and at the same time a blood sample was obtained for measurement of the progesterone level. Patients with apparently normal ovarian function were selected and divided into two groups. Group I (n = 20) comprised all women with a regular cycle of 25 to 35 days, a hyperthermic plateau on the BBT chart lasting 12 to 15 days, and normal ovaries at laparoscopy. Infertility in these women was explained either by tubal occlusion or by sterility of the husband. Group II (n = 22) comprised women with apparently normal uterine, tubal, and ovarian function and apparently fertile husbands, but unexplained infertility. Dating of the endometrial biopsies, in ignorance of all other data, was done (P. G. and J. L.) according to the criteria of Noyes et al.[6] and Dallenbach-Hellweg.[7] Luteinizing hormone[8] and 17β-estradiol[9] were determined by radioimmunoassay. The standards used for LH were the MRC 68-40 and LER-907 preparations. By radioimmunoassay 1 ng of LER-907 corresponded to 42 to 50 IU of LH (MRC 68-40). Means and standard deviations of the hormone concentrations were calculated after logarithmic transformation.[10] Statistical significance was evaluated by Student's paired and unpaired t-test and by the F-test.

RESULTS

In group I the duration of the luteal phase, defined as the interval between the LH peak and the 1st day of subsequent menstruation, was 13.4 ± 0.7 days. In group II it was 13 or 14 days by definition. The LH peak preceded the first significant rise in basal body temperature ($P < 0.05$) by 1 day in group I and by 2 days in group II. Plasma 17β-estradiol concentrations declined significantly ($P < 0.01$) on the day of the LH peak in both groups (Fig. 1). Plasma progesterone levels at the time of biopsy were within normal limits in both groups.

The dating of the endometrial biopsy correlated with the day of the cycle (days after the LH peak) with standard deviations, respectively, of 1.2 and 1.3 days in group I and II (Fig. 2). In the two groups taken together, the standard deviations were not significantly different when the endometrial biopsy was correlated with the LH peak (SD = 1.2 days) or with the onset of the BBT rise (SD = 1.6 days).

DISCUSSION

The usefulness of endometrial biopsies for the evaluation of luteal function can be assessed only by accurate timing of ovulation during the menstrual cycle. According to Noyes and Haman,[5] dating of the endometrium is accurate to within 1 day in 60% of cases. This could be an underestimation of the potential value of endometrial biopsy dating, because Noyes and Haman based their evaluation on BBT charts and menstrual cycles. In the study here reported, patients were selected on the basis of regular cycles, a recurrent hyperthermic plateau of 12 to 15 days' duration, and normal ovaries at laparoscopy. They were divided into a group with explanation for their infertility and a group without explanation. The first group was considered to have normal ovarian function, while the second group could have included some women with presumed luteal phase insufficiency. By taking the LH peak as the point of reference, standard deviations of 1.2 and 1.3 days around

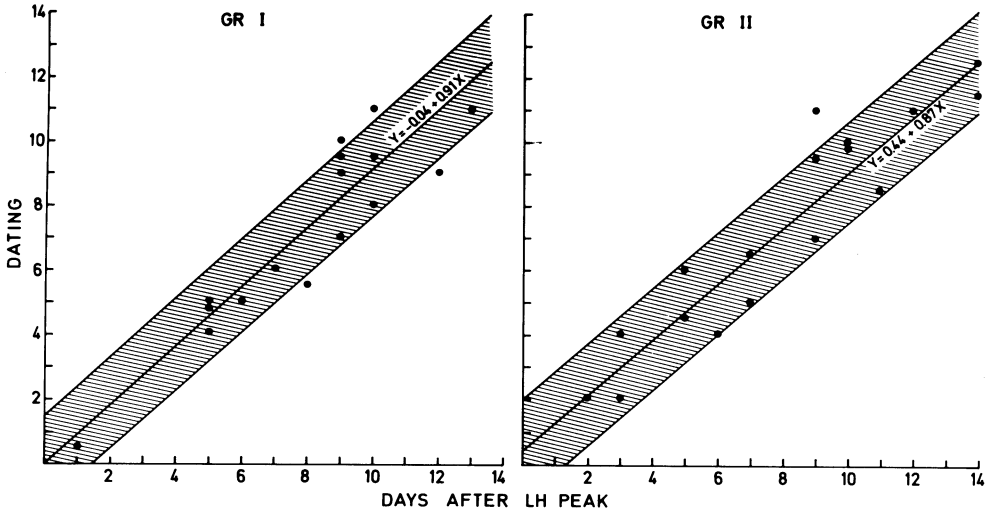

FIG. 2. Dating of the endometrial biopsy in comparison with the LH peak in group I (control group) and group II (women with unexplained infertility). The regression line with 2 SD is indicated.

the linear regression were found in groups I and II, respectively. The findings of Noyes and Haman[5] were thus essentially confirmed, emphasizing that in endometrial biopsy dating a deviation of up to 2 days (2 SD) from the actual day of ovulation is a consequence either of biologic variation in endometrial changes and/or of histologic interpretation.

It is interesting to note that the only difference between the two groups with regard to luteal function was that the onset of the luteal phase occurred somewhat later after the LH peak in group II.[11] The duration of the luteal phase, defined as the interval between the LH peak and the 1st day of subsequent menstration, was 13.4 days in group I, which confirms the findings of Tredway and collaborators.[12] Ovulations therefore preceded menstruation by about 12 to 13 days, since the former followed the LH peak by at least 12 to 24 hours.[13] In both group I and group II the BBT was significantly elevated the day following the LH peak. However, in the individual woman the progressive rise in BBT over several days can make it difficult or impossible to determine accurately the moment of ovulation, and determination of the LH peak would certainly be an advantage from that point of view.

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